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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/158,982	09/23/1998	BRIAN R. BULLARD	029623-0129	4595

23370 7596 02/08/2003

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EXAMINER

MARSCHEL, ARDIN H

ART UNIT	PAPER NUMBER
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1631

2 0

DATE MAILED 02/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/158,982

Applicant(s)

Bullard et al.

Examiner

Ardin Marschel

Art Unit

1631



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

Extensions of time may be available under the provisions of 37 CFR 1.136. In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.

If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.

If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.

Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. 35 U.S.C. § 133.

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704 b.

## Status

1) ☒ Responsive to communication(s) filed on 6/3/02 and 1/16/03

2a) This action is **FINAL**.

2b) ☒ This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

4) ☒ Claim(s) 3, 6-21, and 23

is/are pending in the application.

~~4) ☒ Claim(s) 1, 2, 4, 5, 22, and 24 have been canceled.~~

~~are withdrawn from consideration~~

5) Claim(s) \_\_\_\_\_

is/are allowed.

6) ☒ Claim(s) 3, 6-21, and 23

is/are rejected.

7) ☒ Claim(s) 3 and 6

is/are objected to.

8) Claims \_\_\_\_\_

are subject to restriction and/or election requirement

## Application Papers

9) The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on 1/16/03 is/are ☒ accepted or ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some\* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and or 121.

## Attachment(s)

1 ☒ Notice of References Cited PTO-892

4 ☒ Interview Summary PTO 413 Paper No s 25

2 Notice of Draftsperson's Patent Drawing Review PTO-948

5 Notice of Informal Patent Application PTO-152

3 Information Disclosure Statement s PTO-1449 Paper No s \_\_\_\_\_

6 Other \_\_\_\_\_

The amendment, filed 6/3/02, has been approved for entry and has been entered.

Applicants' arguments, filed 6/3/02, have been fully considered and they are deemed to be persuasive to overcome the rejections of record in a timely manner, leaving at that time no rejections yet pending. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Upon reconsideration, however, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Due to the newly applied rejections and/or objections summarized below, the finality of the Office Action, mailed 12/3/01, is hereby withdrawn.

#### LACK OF ENABLEMENT

Claims 3, 6-21, and 23 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1410 at 1404 (CAFC 1988). The factors to be considered in determining whether undue

experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant invention is apparently directed to gene expression profiling but lacks any instant guidance as to what is performed to use the instant invention. For example, applicants indicate in claim 17 that diagnosis is a possible usage of the instant invention, but lacks any instant guidance therefor. It is noted that microarrays are being generated in the art with frequently thousands of probe sequences thereon, but that interpretation of the results of experiments have been difficult and unpredictable, largely due to the myriad of data points to reconcile. Stoeckert, Jr. et al. discusses the generation of data from microarray analysis and concludes in the final paragraph on page 473, that the "wealth of biological data...has yet to be realized" and the adoption of standards is "a major

step toward making such discoveries a reality". Thus, even as late as the publication of said reference in 2002 the usage of gene expression profiles such as generated on microarrays are unpredictable and lacking in enablement due to being research "yet to be realized" as to uses thereof. It is additionally noted that none of the gene expression profiles in the instant claims are limited to contain even at least one polynucleotide which is known to be of diagnostic value.

#### VAGUENESS AND INDEFINITENESS

Claims 3 and 6-21 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 depends from canceled claim 1 and therefore is vague and indefinite as to what is meant regarding limitations therein. Clarification via clearer claim wording is requested. Claims dependent, directly or indirectly from claim 13, are also rejected hereinunder to this said dependence.

In claim 6, last 2 lines, polynucleotides are described as being "cDNAs or fragments thereof" and are "3'-end fragments of restriction enzyme cleaved cDNAs". As written these characterizations may be reasonably interpreted as only characterizations without any method steps required in the instant claims as possibly implied by these limitations.

Alternatively, the claims are interpretable as being vague and indefinite as to whether these limitations are merely characterizations of polynucleotides as cited previously in claim 6 or are required action steps in order to practice claim 6. Clarification via clearer claim wording is requested. Claim 7 also contains this unclarity due to its dependence from claim 6. This unclarity as to whether a limitation is a characterization or an actual method step is present in claim 10 wherein the generation of fragments is described but this is not worded therein as clearly being an active step or not.

In claims 11 and 12, part (2) of each claim, first and second profiles are cited but without clear antecedent basis due to the claim lacking a previous citation of either a first or second profile. Clarification via clearer claim wording is requested. Similarly, claim 13 cites first and second profiles without clear antecedent basis.

Claim 21 is vague and indefinite as to what is meant for weighting usage therein where a difference between is already a relative magnitude. Clarification via clearer claim wording is requested.

In claim 3, last line, the limitation a "measure of size" is present but is vague and indefinite in that the claim does not indicate what is being measured for size. Is it a measurement of each of the polynucleotides in a profile? Is the size a

measurement of display space? Is the size a measurement of hybridization probe utilized for gene expression profiling, or, is it a measure of the target polynucleotide whose expression is being profiled? Clarification via clearer claim wording is requested. This undefined size measurement is also present in claims 7-10 either directly or via claim dependence.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(b) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 6 and 23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Farr et al. (P/N 5,811,231) in view of the legal decision of In re Venner (120 USPQ 192 et seq.).

In the abstract of Farr et al. the measurement of

transcription or translation levels from genes is disclosed as related to various stress promoters and/or the action of a compound at the subcellular level. These are measurements of gene expression profiles as set forth in the instant claims. Figures 1-11 of Farr et al. display said gene expression in a perspective 3-Dimensional manner with parameters for each expression level in the third dimension. One characteristic parameter is concentration of a compound which may alter gene expression and another is an identifier of a stress promoter being evaluated regarding the gene expression. These stress promoters are discussed, for example, in column 7, line 46, through column 14, line 13. Examples 1-32 in columns 22-32 discuss some exemplary procedures by which to determine gene expression from the expression characteristics for the gene being analyzed regarding promoter activity. The perspective 3-D graphs of the results are displayed as summarized in column 3 for the Figures 1-11. The difference between these studies and the instant claims is the usage of computer or automation practice by which to process the data. These automation practices only replace manual activities and are not a patentable distinction as evidenced by the legal decision of *In re Venner* (120 USPQ 192). This legal decision at page 194, second column, item [6], states that it is well settled that providing a mechanical or automatic means to replace manual activity is not an invention. Thus, as



explained further in said decision, there is no patentable distinction in replacing manual activity with an automatic means as instantly claimed.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the instant invention because Farr et al. describes the data analysis and display of the instant invention which as noted above is obviously computerized as motivated for efficiency if desired via In re Venner.

The above is a reiteration of the basis in Farr et al. for a 3-dimensional representation and display of gene expression data. Instant claim 6 is newly rejected based on Farr et al. because it has been reconsidered to merely characterize polynucleotides in the last 2 lines therein. See the above rejection under 35 U.S.C. § 112, second paragraph, regarding alternative interpretations of instant claim 6. If claim 6, last 2 lines, are merely characterizations of polynucleotides, then their structure as characterized thereby is reasonably viewed as being those as in Farr et al. due to the below analysis. It is noted that the examples in Farr et al. discuss the chemical synthesis of polynucleotide probes, but cite the stress polynucleotides as being characterized in column 8, line 18, through column 16, line 58. Consideration of these polynucleotides results in their structure as corresponding to the last 2 lines of instant claim

6. The multitude of stress polynucleotides in said Farr et al. listing is reasonably characterized by starting in column 8, lines 24-53, as describing the first three polynucleotides which thus establish the basic trend of the structure of the lengthy list in Farr et al. Included with the Office Action are copies of the first three polynucleotide references in said column 8, lines 24-53, discussion which characterize these first three polynucleotides. For the first polynucleotide type, Sogawa et al. [PNAS 83:8044(1985)] on pages 8044-8045, bridging paragraph and in Figure 1 describe inserts in plasmids which are restriction enzyme cleavage products and which have 3'-termini as all such polynucleotides do. The second Farr et al. polynucleotide type is described in Rushmore et al. [PNAS 87:3826(1990)] on page 3826, second column, lines 20-43, as being cloned via restriction enzyme cleavage and as above have 3' termini. The third Farr et al. polynucleotide type is described in de Groot et al. [EMBO Journal 10(3):2523(1991)] on page 2530, second column, in the section entitled "Cells and Plasmids" as also being cloned via restriction enzyme cleavage and also have 3' termini as required for such polynucleotide fragments. Thus, in summary, the Farr et al. description of three values which are displayed in multi-dimensional display of polynucleotide expression is suggested as being a computerized display in view of In re Venner thus suggesting and motivating the instant

invention. Claim 23 is included herein due to a reevaluation of a delta plot in the last lines as being inclusive of the histogram or bar plots in Farr et al.

The disclosure is objected to because of the following informalities:

In claims 3 and 6, lines 1 of each claim, the phrase "analyzing an displaying" apparently contains a misspelled "an" in context.

Correction is required.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

*Ardin H. Marschel*  
ARDIN H. MARSCHEL  
PH.D.

February 3, 2003